REMARKS

This Amendment is presented in Response to the Office Action which issued May 29, 1997 in this case. Included with this Amendment is a Petition For Extension Of Time, to extend Applicant's time to Respond to the May 29, 1997, Office Action, through and until October 29, 1997. A check made out to the Assistant Commissioner for an amount of $190.00 accompanies this Petition to cover the Petition fee. Hence, claims 11-16 and 27-32 have been deleted without prejudice or disclaimer of subject matter, the Specification, and claims 1, 18, 35 and 37 are amended hereby, and new claim 39 is now presented. After amendment, claims 1-10, 17-26 and 33-39 are pending, where claims 1, 18, 35, & 37 are the independent claims.

Initially, Applicants respond to the Notice of Draftspersons Patent Drawing Review, PTO 948, which accompanied the May 29th Office Action. Applicants respectfully request that the Examiner hold the stated objections to the drawings in abeyance until a notice of allowance issues in this case, at which time formal drawings will be submitted.

In the Office Action, Claims 1-38 were rejected under 35 U.S.C. δ 112, first paragraph, as containing subject matter not described in the specification in a sufficiently enabling manner. The Examiner asserts that it is unclear from the specification: (1) whether CATEZOMES™ as recited on Page 6 are liposomes made of instant lipids; and (2) whether the liposomes are commercially available. The Examiner further asserts that if a fatty acid ("A") is already linked to the amino group ("DDA"), as recited on Page 6, it is unclear how one can react another fatty acid with this compound to obtain a salt, and that the manner in which methodology is recited is confusing, and that the examples do not clarify the confusion.

In Response, applicants have amended the portions of the specification on Page 6 referred to by the Examiner, to more clearly recite that CATEZOMES™ is a trademark

used by Applicant to qualify its cationic liposomes in the minds of consumers. For that matter, applicants respectfully direct the Examiner's attention to pages 9 to 11 of applicants' detailed description, at which applicants' methodology clearly states that its CATEZOMES™ liposomes are lipids comprised of materials recited in the specification, and, as such, are not commercially available, as is, for example. A-ADDA, one of the constituents of applicants' cationic liposomes.

In further response, applicants respectfully assert that their description of the preferred embodiment on Page 6 is **incomplete** if read out of context with the first paragraph on that page, and the conclusion on page 7. That is, page 6, line 1 begins: "In one preferred embodiment," which continues its description of the preferred embodiment, i.e., cationic liposomes through page 7, line 18. The three paragraphs read together describe the invention.

Hence, by reading the summary of the invention, as recited by the "complete" three paragraph section, it is respectfully believed that the section describes clearly applicants' cationic liposomes. Applicants further assert that after reading of the whole section, it will become clear that the salt bridge (or bond) is formed between a quaternary amine group of the ADDA[1] and a carboxyl group of the fatty acid called out, resulting in A-ADDA, one of the constituents used by applicants in their invention. Applicants respectfully assert that the methodology recited, as amended, is not confusing to one skilled in the art, and according assert that the claims are in compliance with section 112, first paragraph.

Claims 1-38 were also rejected in the Office Action under 35 U.S.C. δ 112, second paragraph, as indefinite with regard to Applicants use of the acronym "A-ADDA", and because claims 1-38 do not recite additional fatty acid, as does the Specification. In particular, the Examiner refers to Claim 35 as not clearly reciting a

[1] the ADDA being the alkyl chain to which a first fatty acid such as behenic acid is attached

compound which forms the bi-layers. The Examiner further asserts that "said load material" in Claims 2 & 3, and "said buffer" in Claim 3 have no antecedent basis in Claim 1, that it is unclear what Applicants intend to convey by "said buffer dispersing includes H_2O" in Claims 4 & 21, and that "includes" is indefinite in Claims 4-7, 9, 17, 21-23, 26 & 33-35.

The Examiner also asserts that, in a section 112, second paragraph context, it is unclear what Applicants intend to convey by "applying sufficient specified dimension in Claims 9 & 26", that Claim 10 should adequately recite how A-ADDA is prepared, and that the term "around" in Claims 10, 11, 27 & 28, and "about" in Claims 14 & 31 should be deleted. The Examiner further asserts that it is unclear what "claims" in Claim 12 is intended to convey, what is meant by a "occurrence of a triggering condition in Claim 35", that it is unclear where the "proteins" are and how they readily adhere, as recited in Claim 36, that it is unclear what controlling the salt bridge means in Claim 37, and that it is suggested to delete the "one of" in Claims 35 & 38 to recite a Markush format in lieu of same.

In Response, Applicant asserts that the claims are now fully in compliance with 35 U.S.C. δ 112, second paragraph. Applicants have amended the claims to more specifically recite the proper chemical name for the acronym "A-ADDA". Claims 11-16 and 27-32 have been deleted. Claims 4 and 21 have been amended as suggestion, and sufficient mechanical force necessary to form the liposomes is described in the references referred to in the specification. Claims 1-7, 9, 17-18, 21-23, 28, 35 and 37 have been amended to now recite "comprises" in lieu of the word "includes".

Next, applicants respectfully point out that the claims reciting A-ADDA are definite. The claims do not rely on a process of preparing the A-ADDA, that is, a fatty acid held by salt bond to an acyl N_n, N_n-dimethyl-1, n-diamino alkyl (ADDA), as described at page six of the Specification, but for preparing lipid vesicles and/or a liposomal delivery system. Since A-ADDA may be purchased, in situ, the claims do not

recite preparation of the A-ADDA, and therefore, do not refer to the fatty acid which is attached to DDA in the preparation (by commercial suppliers of A-ADDA).

Further, applicants have amended claim 1 to clearly recite that A-ADDA is mixed with a load material in a buffering solution and acted upon to realize a dispersion. Applicants, therefore believe that claims 2 and 3 are now definite. Still further, claim 4 has been amended to replace "H_2O and said alkylammonium fatty acid salt is", with --dispersing--. That is, claims 4 as amended now reads: "The method defined by claim 1, wherein said step of dispersing includes a trialkylammonium fatty acid salt." Consequently, applicants assert that by deleting claims 11-16 and 27-32 and the amendments implemented, that claims 7, 9, 17-18, 21-23, and 33-35 are now in compliance with Section 112, second paragraph.

Claims 18-38 were rejected under 35 U.S.C. δ 102 (b) in the Office Action as being anticipated by European Patent No. 0158,441 to Phares Pharmaceutical Research of the Netherlands. The Examiner asserts that the specification on Page 6 appears to indicate the commercial availability of the claimed liposomal composition, and the method by which it is prepared has no significance in composition claims in the absence of showing a patentably significant difference between the available product and the claimed product. The Examiner asserts further that the Phares Patent teaches a liposomal composition containing instant lipid (note the abstract, and examples).

In Response, Applicants assert that Claims 18-26, and 33-38 (and newly presented claim 39) are patentably distinct from the invention disclosed in EP 158,441. More particularly, EP 158,441 discloses compositions based on membrane lipids, and dispersions of same. Where EP 158, 441 recites that phospholipid vesicles, which are also know as liposomes, the patent refers to phospholipic-comprised vesicles as a species, and not the genus liposomes. That is, Phares discloses phospholipid liposomes, to the exclusion of, for example, surfactant based liposomes. Applicants' liposomes are formed of A-ADDA and an active to realize an A-ADDA liposomes with a slightly positive

surface charge. Hence, applicants respectfully assert that their invention as claimed is patentably distinct from Phares.

Claims 18-38 were rejected under 35 U.S.C. δ 103(a) in the Office Action as being unpatentable over U.S. Patent No. 5,494,803 to Carbonell. The Examiner asserts that Carbonell teaches that Di- and Tri- alkyl quaternary ammonium salts are routinely used in the preparation of liposomes (Column 4, line 60), and the use of instant quaternary ammonium compounds, therefore, in the absence of showing unexpected results, would have been *prima face* obvious to one skilled in the art.

In Response, Applicants respectfully assert that claims 8-38 are patently distinct from Carbonell for at least the following reasons.

Carbonell discloses immunodiagnostic assays, comprised of liposomes formed for the express purpose of carrying detectable markers in the liposomal bilayers, covalently bonded with the outside layers of same to perform the test. While column 4, line 60 does refer to the use of di- and tri-alkyl quaternary ammonium salts, applicants assert that Carbonell uses same only as a cheap and readily available liposome raw material, i.e., surfactants. Nothing in the '803 patent teaches utilizing surfactants to realize a positive surface charge on the resultant liposome-based assay (see col. 6 of the '803 patent). Hence, applicants claims cannot be obvious in view of the '803 patent, and so the rejections to the claims based on same are now obviated.

In the Office Action claims 1-38 were rejected under 35 U.S.C. δ 103 as unpatentable over Japanese Patent No. JA 57-82311 to Janebi Seiyaku, in view of the '803 patent. The Examiner asserts that the Japanese Patent teaches a process for preparing liposomes using phospholipids which involves dispersing a lipid in an aqueous medium and subjecting the medium to high shear processing. The Examiner further asserts that although the Japanese patent reference teaches the use of other synthetic lipids, that it does not specifically teach the use of the instant compounds, but that Carbonell teaches

the use of Di- and Tri-alkyl quaternary ammonium salts as asserted. The Examiner then concludes that the use of such salts, with the expectation of obtaining similar results, would have been *prima face* obvious to one skilled in the art in view of the same.

In Response, Applicants assert that Claims 1-38 are patentably distinct from Japanese Patent reference, JA 0082311, in view of the '803 patent because Carbonell teaches assays delivery of active substances by inserting same within the liposomal bilayers. The actives are, therefore, are reactant chemically or covalently, as distinguished from applicants' claimed invention. The present invention utilizes a salt bond to maintain or dissolve a salt bond use to form applicants' cationic liposomes. There is no teaching or suggestion in either the '803 patent or the Japanese reference to use a salt bond to realized a liposome which can deliver its load on cue. Hence, applicants respectively assert that claims 1-10, 17-26 and 33-39 are non-obvious in view of the Japanese reference, whether taken alone or in combination with the '803 patent.

It is respectfully asserted that this amendment responds fully to the May 29 office action and applicants therefore request allowance of claims 1-30.

Respectfully yours,

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